The Influence of Mechanical Loading Frequency on Tissue Adaptation

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Mechanical deformation serves as a critical input in the development and adaptation of many tissues. This phenomenon is perhaps most obvious in the skeletal system. Starting in the late nineteenth century, investigators have attempted to correlate the specific functions of skeletal components with the form of these biomechanical structures. Yet, significant progress in this area was restricted by a lack of meaningful quantitative data to describe the functional activity. The development of mechanical strain gages which can be implanted *in vivo* has eliminated this restriction. The introduction of these devices, coupled with that of well controlled animal models of adaptation, has provided the data that now permits a careful analysis of the specific aspects of mechanical activity to which cells will respond.

Strain gage recordings from the long bones of animals have demonstrated that two distinct forms of functional activity occur in the skeletal system. During locomotion, large (up to 5000 microstrain) deformations occur in bones, but these strains occur at relatively low frequencies. Fundamental strain frequencies are found to be between 1 and 3 Hz, consistent with typical stride rates, and harmonics multiples of fundamental can be identified up through 15 Hz. Conversely, the distinctive skeletal strains associated with postural muscle activity are quite small (on the order of 100 microstrain) and occur at a relatively high frequency. During standing, records from the long bones of the leg demonstrate distinct strain oscillations between 25 and 30 Hz, with the almost complete absence of strain information at lower frequencies. While the locomotory strains are large, the exposure duration for normal activity is quite short. This can be contrasted to postural activity for which small strain magnitudes exist over long durations.

In order to address the relevance of these two distinct functional activities, and the extent to which the cells within bone tissue can utilize these two different strain signals for adaptation, we have undertaken a series of controlled mechanical loading experiments utilizing the isolated avian ulna model of adaptive bone remodeling. Using low frequency (0.5 Hz), large magnitude (2000 microstrain) loads of varying duration, we have found that bone tissue will respond maximally if the loading duration exceeds 60 seconds. Using contant duration (360 second), small magnitude (500 microstrain) loads of varying frequency, we have found that the bone tissue responds to increasing frequency in a monotonic manner up through 30 Hz.

These results identify a classic resolution-integration paradox in the ability of bone cells to detect mechanical strain. The cells require up to 60 seconds to fully respond to the mechanical strain suggesting a temporal integration time constant on the order of 10 seconds. However, the cells are fully capable of detecting 30 Hz strains, suggesting a temporal resolution on the order of 10 milliseconds. In order to attain both this temporal integration ability and the high resolution requires at least a two stage detection scheme. That is, mechanical strain signal detection is not direct, but utilizes a higher level of processing. This processing may be based on some form of spatial integration of the strain information.